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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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KNOBBE MARTENS OLSON & BEAR LLP
2040 MAIN STREET
FOURTEENTH FLOOR
IRVINE, CA 92614

EXAMINER	
ALLEN, MARIANNE P	

ART UNIT	PAPER NUMBER
1631	

DATE MAILED: 11/20/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/923,870	PALSSON, BERNHARD	
	Examiner	Art Unit	
	Marianne P. Allen	1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 24-48 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 24-48 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on 23 April 2003 is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1)☒ Notice of References Cited (PTO-892)

2)☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)

3)☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 4/23/03 (1 page)

4)☐ Interview Summary (PTO-413) Paper No(s). _____.

5)☐ Notice of Informal Patent Application (PTO-152)

6)☐ Other: .

DETAILED ACTION

Claims 1-23 have been cancelled. Claims 24-48 have been newly added and are under consideration by the examiner.

Applicant's arguments filed 4/23/03 and 8/27/03 have been fully considered but they are not persuasive.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Drawings

The replacement drawing for Figure 2 was received on 4/23/03. This drawing is acceptable.

Oath/Declaration

This application presents a claim for subject matter not originally claimed or embraced in the statement of the invention. A supplemental oath or declaration is required under 37 CFR 1.67. The new oath or declaration must properly identify the application of which it is to form a part, preferably by application number and filing date in the body of the oath or declaration. See MPEP §§ 602.01 and 602.02. This requirement is maintained for reasons of record. The claims originally filed in the instant application did not correspond to the claims originally filed in the parent application. These claims could not have been introduced into the parent application without a rejection with respect to new matter. Applicant's arguments are not agreed with for basis in the specification for the claims originally filed in this application. It is not relevant whether the claims originally filed in the instant application are pending or canceled

or whether the current claims under examination find support in the specification as filed. As filed, the instant application was a continuation-in-part of the parent application.

Claim Rejections - 35 USC § 101

Claims 41-48 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter.

Claim 41 is directed to a system for representing metabolic reactions comprising a metabolic network comprising a table of reactants and products. This system is a data product. Dependent claims 42-48 are considered process limitations that define how the content of the table of reactants and products is produced. This does not alter the fact that claims 41-48 are directed to data which is non-statutory subject matter.

Claim Rejections - 35 USC § 112

Claims 24-48 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. This is a new matter rejection rejection.

Claim 24 is directed to a method for creating a metabolic network representing metabolic reactions comprising providing a table of reactants and products, selecting a nucleic acid sequence corresponding to a gene of unknown function, determining whether the nucleic acid corresponds to a metabolic gene, and if so, adding the reactants, products, and stoichiometry to the table of reactants and products to create a metabolic network. As written, this claim is interpreted to mean that the metabolic network created is a merely a table of reactants and products.

Claim 33 is directed to a system for providing a metabolic network comprising a table of reactants and products, a first process, and a second process. As written, this claim does not make clear whether the first and second processes are considered to be mental actions, hardware, software, or something else. The physical components of the system are unclear, particularly in view of dependent claim 36 reciting "said method is performed by a computer." Note that claim 33 is not directed to a method and does not recite "method." Note that dependent claims 37-40 add limitations of applying constraints or performing a flux balance but that these limitations do not further limit the system in any way. That is, they do not clearly add structural or functional components to the system.

Claim 41 is directed to a system for representing metabolic reactions comprising a metabolic network comprising a table of reactants and products. As written, this claim does not make clear whether the table of reactants and products are in the form of paper text, hardware, software, or something else. The physical components of the system are unclear, particularly in view of dependent claim 44 reciting "said method is performed by a computer." Note that claim 41 is not directed to a method and does not recite "method." Note that dependent claims 45-48 add limitations of applying constraints or performing a flux balance but that these limitations do not further limit the system in any way. That is, they do not clearly add structural or functional components to the table of reactants and products.

The specification does not provide support for the present claims. Applicant points to portions of the specification in the response filed 8/27/03; however, while particular words or phrases recited in the claims may be found in different parts of the specification, the concepts of the method and systems as claimed are not. The summary of the invention is directed to

constructing metabolic genotypes and genome specific stoichiometric matrices from genome annotation data. The genome sequence, the annotation data, and the biomass requirements of an organism are used to construct genomically complete metabolic genotypes and genome-specific stoichiometric matrices. The matrices are analyzed using a flux-balance analysis. (See pages 4-5.) The format of matrix is discussed on page 9. The claims as written do not correspond to these descriptions nor the flow charts in the figures. In particular, the claimed metabolic network does not correspond to the disclosed metabolic genotype or genome specific stoichiometric matrix. There is no disclosure of a method of creating a metabolic network with the recited steps nor the systems for providing or representing such a network. Furthermore, a fair reading of the specification indicates that a network is more than a table of reactants and products from metabolic reactions. It is for example, an in silico microbial strain produced by the process of Figure 2. In particular, the specification does not contemplate implementations that do not involve a computer (see claims 27, 36, and 44.) For example, there is no disclosure of homology analysis by hand. (See page 7 which discusses various computer algorithms that would be used.)

The specification as originally filed would not reasonably convey to one of ordinary skill in the art that the invention as presently claimed was contemplated.

Should this new matter rejection be overcome, at least the following enablement rejection would apply.

The specification does not inform one of ordinary skill in the art how one would know if a nucleic acid sequence corresponds to a known metabolic gene nor how to determine what its

reactants, products, and stoichiometry would be. Note that the table required by the claims requires only reactants and products but not stoichiometry.

The claims require a table of metabolic reactions known to take place in the organism wherein the products of at least one metabolic reaction are linked to the reactants of another metabolic reaction. These reactions and the pathways to which they belong are not known for a large number of organisms. In many cases, knowledge of an enzyme present in an organism does not provide any information as to how this enzyme fits into the metabolic network. As such, one would be required to determine and develop such a table for the organism of interest. This constitutes undue experimentation as there is no guidance on developing such a table.

In addition, the specification does not provide guidance on how assignment of function would then provide the metabolic reaction of the candidate metabolic gene. That is, assigning the function of a kinase based upon homology does not provide the substrate and product of the reaction. The specification provides absolutely no guidance as to how these should be determined. What degree of homology leads to the conclusion of corresponding to a known metabolic gene?

With respect to claim 28, for example, it is not known what positive and active steps must be performed to apply constraints on said metabolic network that reflect the metabolic requirements of said organism. Applicant is reminded that according to claim 24 the metabolic network is merely a table of reactants and products.

With respect to claim 29, for example, how does one perform flux balance analysis on a table of reactants and products? It appears that more information is required for such analysis. What results would cause one to infer that the organism can or cannot survive?

With respect to claim 32, for example, it is not known what positive and active steps must be performed to represent the metabolic network as a stoichiometrix matrix. Applicant is reminded that according to claim 24 the metabolic network is merely a table of reactants and products.

As set forth in the prior Office action, it is maintained that the specification lacks guidance in setting forth reasonable means for assigning a function based on a homology comparison. Applicant has referred to Edwards et al. (PNAS, 2000) and Edwards et al. (JBC, 1999) on page 16 of the response. Applicant asserts that they were published after the filing date and as such would not have been known in the art at the time of this invention to provide guidance to one practicing the claimed invention. Furthermore, while these references discloses assembling information regarding metabolic reactions from a variety of sources (literature, annotated databases), there is no explanation as to any criteria used to assign function based on a homology comparison. If applicant believes otherwise, they are invited to point to the particular portions of these references where it is discussed.

Claims 28-31, 37-40, and 45-48 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 28-31 are confusing in adding steps that do not clearly further limit the method of creating a metabolic network. That is, they perform analysis that is not directed to creating the network. As such, the resulting method is no longer consistent with the preamble goal of claim 24. See also claims 37-40 where these limitations do not change the system components and 45-

48 where these limitations do not change the content of the table of reactants and products. Each of these claims fails to further limit the independent claim.

Claim 48 depends upon claim 41; however, there is no antecedent basis for constraints in this claim.

Claim Rejections - 35 USC § 102

Claims 24-48 are rejected under 35 U.S.C. 102(b) as being anticipated by Edwards et al. (Journal of Biological Chemistry, June 1999).

Applicant is entitled to only the instant filing date of 8/6/01 and not the filing date of parent application 09/243,022 for the reasons set forth in the prior Office action.

Edwards et al. discloses determining six optimal phenotypes from the same metabolic genotype using different constraining features for *Haemophilus influenzae* Rd. Some metabolic genes used in the analysis had function assigned based upon homology to known genes. Flux balance analysis was used with linear programming. See abstract and materials and methods. Conditions for optimal growth and minimal media were determined using constraints. See results and Figure 2.

Claims 41-48 are rejected under 35 U.S.C. 102(b) as being anticipated by Stryer.

As set forth above, claims 41-48 are considered to be directed to a product by process. Applicant is reminded that a product by process claim is examined as a product irrespective of the manner in which the product is produced. The claimed product is a table of reactants and products.

Table 13-1 of Stryer provides a table of metabolic reactions (including stoichiometry) for the citric acid cycle. According to the limitations of the claims, this table could have been generated or produced by the process steps and as such Table 13-1 anticipates the claimed product. Applicant is reminded that claims 45-48 do not change the content of the table.

Conclusion

No claim is allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Marianne P. Allen whose telephone number is 703-308-0666. The examiner can normally be reached on Monday-Thursday, 5:30 am - 1:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Woodward can be reached on 703-308-4028. The fax phone number for the organization where this application or proceeding is assigned is 703-305-3014.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Marianne P. Allen
Primary Examiner
Art Unit 1631

mpa